REMARKS

Claims 1-10 were pending. Claims 3, 4, 6 and 7 have been amended. Claims 1-2 and 5 are canceled, and new claim 16 is added. No new matter is added. Applicants respectfully request reconsideration of the rejections and allowance of Claims 3-4, 6-10, and 16.

Support for the language of Claim 16 may be found in the specification, paragraph 35.

Claim 3 and claims dependent thereupon have been rejected under 35 U.S.C. 112, first paragraph as lacking enablement are rejected under 35 U.S.C. §112, first paragraph. Applicants respectfully submit that one of ordinary skill in the art could practice the claimed invention.

Claim 3 is directed to a polynucleotide encoding the amino acid sequence set forth in SEQ ID NO:2. Enablement is judged in view of the level of skill in the art. The degeneracy of the genetic code has been well known for nearly 50 years, and tables providing the codon for every amino acid sequence are readily available from public sources. Given the amino acid sequence, one of skill in the art could readily prepare a nucleotide sequence encoding SEQ ID NO:2. The level of skill required for such an undertaking would be very low, and certainly routine.

Applicants respectfully submit that one of skill in the art could readily produce a polynucleotide encoding the amino acid sequence of SEQ ID NO:2. Withdrawal of the rejection is requested.

New Claim 16 is directed to nucleic acids encoding a polypeptide that is 98% identical to SEQ ID NO:2. Applicants respectfully submit that such a nucleic acid meets the requirements of 35 U.S.C. 112.

The law regarding enablement of inventions is clear: "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."1

The scope of enablement must only bear a "reasonable correlation" to the scope of the claims (MPEP §2164.08) and the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled (MPEP §2164.08(b)). The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be

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1 *United States v. Telectronics, Inc.*, 8 USPQ 2d 1217, 1233 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989). See also *Genentech, Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (Fed. Cir. 1997), *cert. denied*, 522 U.S. 963 (1997); *Scripps Clinic and Research Foundation v. Genentech, Inc.*, 18 USPQ 2d 1001 (Fed. Cir. 1991).

inoperative or operative with expenditure of no more effort that is normally required in the art (MPEP §2164.08(b)).

The specification describes the subject molecules as a CaM kinase, a well-known family of enzymes (see paragraphs 7-10 of the specification). As such, the Applicants respectfully submit that the general state of the art with respect to CaM kinase proteins is exceedingly high.

The Applicants respectfully submit that in view of the above information, a skilled person would know which amino acids of SEQ ID NO:2 cannot be changed, and others that could be changed, in order to create a variant that retains the kinase activity.

With respect to satisfying the written description requirement, even in an "unpredictable art," applicants "are *not* required to disclose *every* species encompassed by their claims . . . ."2 Otherwise, to claim a genus, every species within a genus would have to be explicitly described. This is **not** the law. In other words, the written description requirement does not require a specific description of every species encompassed by a claim.

As such, the argument that the specification does not contain any disclosure of the function of **all** the polypeptide sequence encoded by polynucleotides that are 98% identical to SEQ ID NO:2, has no bearing on the instant claims because such a level of disclosure is not required by law.

With respect to the written description guidelines, the guidance set forth in the "Synopsis of Application of Written Description Guidelines", as published to the world wide website of the U.S.P.T.O. on March 1st, 2000 (http://www.uspto.gov/web/offices/pac/writtendesc.pdf), indicates that the claims are adequately described.

Example 14 of the Synopsis describes a scenario that is very similar to that currently under examination. Example 14 provides an example of a specification that discloses the sequence of a polypeptide having the sequence of SEQ ID NO:3, and also discloses that the polypeptide has a certain enzymatic activity. This example also states that the specification also "contemplates but does not exemplify" variants of SEQ ID NO:3, and provides an assay for measuring the activity of the protein. In this example, the claims are directed to polypeptides having a sequence that is at least 95% identical to that of SEQ ID NO: 3 and catalyze the reaction of A→B.

The Synopsis states that the claimed subject matter is adequately described by the specification and the requirements of 35 USC §112 first paragraph have been met because "The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which

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2 *In re Angstadt,* 537 F.2d 498, 502-03, 190 U.S.P.Q. (BNA) 214, 218, (C.C.P.A. 1976).

applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity.

For the Examiner's convenience, Example 14 of the Synopsis of Application of Written Description Guidelines is reproduced below:

Example 14: Product by Function

> **Specification:** The specification exemplifies a protein isolated from liver that catalyzes the reaction of **A B.** The isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO: 3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions is routine in the art and provides an assay for detecting the catalytic activity of the protein.

Claim:

> A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A B.

Analysis:

> A review of the full content of the specification indicates that a protein having SEQ ID NO: 3 or variants having 95% identity to SEQ ID NO: 3 and having catalytic activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art.
>
> A review of the claim indicates that variants of SEQ ID NO: 3 include but are not limited to those variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions; but all variants must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO: 3.
>
> Additionally, the claim is drawn to a protein which **comprises** SEQ ID NO: 3 or a variant thereof that has 95% identity to SEQ ID NO: 3. In other words, the protein claimed may be larger than SEQ ID NO: 3 or its variant with 95% identity to SEQ ID NO: 3. It should be noted that "having" is open language, equivalent to "comprising".
>
> The claim has two different generic embodiments, the first being a protein which comprises SEQ ID NO: 3 and the second being variants of SEQ ID NO: 3. There is a single species disclosed, that species being SEQ ID NO: 3.
>
> A search of the prior art indicates that SEQ ID NO: 3 is novel and unobvious.

There is actual reduction to practice of the single disclosed species.

The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

The Applicants respectfully submit that the fact pattern of the example set forth above is very similar to the instant fact pattern. In other words, the instant specification a) describes the sequence of a full length polypeptide, b) describes that SEQ ID NO:2 is a CaM kinase, c) "contemplate but does not exemplify" variants of SEQ ID NO:2, and d) provides detailed methods of how activity can be assayed.

As such, by the reasoning set forth in the Example 14 of the Synopsis, in combination with the amount of public knowledge on the structure of CaM kinase proteins, the instant claims should be considered adequately described by the specification, meeting the requirements of 35 USC §112, first paragraph.

Claim 3 has been rejected under 35 U.S.C. 102(e) as anticipated by Tang *et al.* Applicants respectfully submit that the rejection is not understood. A review of the disclosure of Tang *et al.* reveals that SEQ ID NO:4 (page 37) of Tang *et al.* corresponds to Genbank accession number AB011102; KIAA0530. A pairwise BLAST comparison of the corresponding amino acid sequence with the amino acid sequence of SEQ ID NO:2 reveals no similarity.

The sequence analysis enclosed with the Office Action discloses a comparison of the sequences of the present invention with Genbank accession number AL023754, submitted by Grafham. Applicants presume this is the sequence the Examiner intended to cite.

A comparison of SEQ ID NO:2 with the amino acid sequence of AL023754 reveals 100% sequence identity up to residue 447. However, from residue 448-476 there is so sequence similarity

between the two polypeptides. In view of the lack of sequence identity, Applicants respectfully submit that Claim 3 is patentable over the cited art. Withdrawal of the rejection is requested.

Claim 3 has been rejected under 35 U.S.C. 102(b) as anticipated by Rhodes et al., EMBL AL049688. Applicants respectfully submit that Rhodes *et al* does not teach a polypeptide comprising the amino acid sequence of SEQ ID NO:2. A pairwise BLAST comparison of the two polypeptide sequences, as shown below, demonstrates a number of amino acid differences:

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Query: 6    MGRKEEDDCSSWKKQTTNIRKTFIFMEVLGSGAFSEVFLVFTKQRLTGKLFALKCIKKSP 65
            MGRKEEDDCSSWKKQTTNIRKTFIFMEVLGSGAFSEVFLV  KQRLTGKLFALKCIKKSP
Sbjct: 1    MGRKEEDDCSSWKKQTTNIRKTFIFMEVLGSGAFSEVFLV--KQRLTGKLFALKCIKKSP 58

Query: 66   AFRDSSLENEIAVLKKIKHENIVTLEDIYESTTHYYLVMQLFTVSGGELFDRILERGVYT 125
            AFRDSSLENEIAVLKKIKHENIVTLEDIYESTTHYYLVMQL  VSGGELFDRILERGVYT
Sbjct: 59   AFRDSSLENEIAVLKKIKHENIVTLEDIYESTTHYYLVMQL--VSGGELFDRILERGVYT 116

Query: 126  EKDASLVIQQVLSAVKYLHENGIVHRDLKPENLLYLTPEENSFTKIMITDFGLSKMEQNG 185
            EKDASLVIQQVLSAVKYLHENGIVHRDLKPENLLYLTPEENS  KIMITDFGLSKMEQNG
Sbjct: 117  EKDASLVIQQVLSAVKYLHENGIVHRDLKPENLLYLTPEENS--KIMITDFGLSKMEQNG 174

Query: 186  IMSTACGTPGYVAPEVLAQKPYSKAVDCWSIGVITYILLCGYPFTPFYEETESKLFEKIK 245
            IMSTACGTPGYVAPEVLAQKPYSKAVDCWSIGVITYILLCGYP  PFYEETESKLFEKIK
Sbjct: 175  IMSTACGTPGYVAPEVLAQKPYSKAVDCWSIGVITYILLCGYP--PFYEETESKLFEKIK 232

Query: 246  EGYYEFESPFWDDISESAKDFICHLLEKDPNERYTCEKALSHPWFTIDGNTALHRDIYPS 305
            EGYYEFESPFWDDISESAKDFICHLLEKDPNERYTCEKALSHPW  IDGNTALHRDIYPS
Sbjct: 233  EGYYEFESPFWDDISESAKDFICHLLEKDPNERYTCEKALSHPW--IDGNTALHRDIYPS 290

Query: 306  VSLQIQKNFAKSKWRQAFNAAAVVHHMRKLHMNLHSPGVRPEVENFTRPPETQASETSRP 365
            VSLQIQKNFAKSKWRQAFNAAAVVHHMRKLHMNLHSPGVRPEVEN  RPPETQASETSRP
Sbjct: 291  VSLQIQKNFAKSKWRQAFNAAAVVHHMRKLHMNLHSPGVRPEVEN--RPPETQASETSRP 348

Query: 366  SSPEITITEAPVLDHSVALPALTQLPCQHGRRPTAPGGRSLNCLVNFTGSLHISSSLVPM 425
            SSPEITITEAPVLDHSVALPALTQLPCQHGRRPTAPGGRSLNCLVN  GSLHISSSLVPM
Sbjct: 349  SSPEITITEAPVLDHSVALPALTQLPCQHGRRPTAPGGRSLNCLVN--GSLHISSSLVPM 406

Query: 426  HQGSLAAGPCGCCSSCLNIGSKGKSSYCSEPTLLKKANKKQNFKSEVFTMVPVKASGSSH 485
            HQGSLAAGPCGCCSSCLNIGSKGKSSYCSEPTLLKKANKKQNFKSEV  MVPVKASGSSH
Sbjct: 407  HQGSLAAGPCGCCSSCLNIGSKGKSSYCSEPTLLKKANKKQNFKSEV--MVPVKASGSSH 464

Query: 486  CRAGQTGVCLIM 497
            CRAGQTGVCLIM
Sbjct: 465  CRAGQTGVCLIM 476
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In view of the lack of sequence identity, Applicants respectfully submit that Claim 3 is patentable over Rhodes et al. Withdrawal of the rejection is requested.

CONCLUSION

Applicants submit that all of the claims are now in condition for allowance, which action is requested. If the Examiner finds that a Telephone Conference would expedite the prosecution of this application, she is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any other fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815, order number KINE-024.

Respectfully submitted,

Date: August 8, 2003

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